REMARKS

Amendments to the Claims

Claims 1-7, 15 and 18-19 have been amended.

New Claims 20-33 have been added.

Claims 8-14 and 17 have been canceled.

Claims 1-3 have been amended to recite "a method of inhibiting TNFα in a human patient having a neurodegenerative disease." Support is found in the specification, for example, at page 16, lines 13-24; page 56, line 28 to page 59, line 10; particularly page 57, line 25 to page 58, line 15. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 39, line 20 to page 40, line 9.

Claims 1-3 has been further amended to recite "antigen-binding fragment." Support is found in the specification, for example, at page 17, lines 2-8. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 1, lines 5-12 and page 11, lines 10-20.

Claims 1 and 3, as amended, recites that the antibody or antigen-binding fragment competitively inhibits binding of A2 (ATCC Accession No PTA-7045) to TNFα. Support is found in the specification, for example, at page 19, line 17 to page 20, line 1; page 25, lines 15-22 and page 30, lines 5-9. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, line 24 to page 13, line 4; page 14, lines 3-9; and page 19, lines 3-10.

Claim 2, as amended, recites "comprises the antigen-binding regions of A2 (ATCC Accession No PTA-7045)." Support is found in the specification, for example, at page 19, lines 1-6; and page 25, lines 15-22. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

Claims 1-3 has been further amended to recite that the antibody or antigen-binding fragment "binds to a neutralizing epitope of human TNFα *in vivo* with an affinity of at least 1 x 10^8 liter/mole, measured as an association constant (Ka), as determined by Scatchard analysis." Support is found in the specification, for example, at page 21, lines 15-22; page 60, lines 8-17; and Example X, particularly at page 80, lines 12-16. In addition, support is found in the

specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 13, lines 5-8; page 18, lines 17-19; page 20, lines 3-6; and Example X, particularly, at page 67, line 12 to page 68, line 25.

Claims 1-2 have been further amended to recite "human constant region." Claim 3 has been amended to recite "human IgG1" constant region. Support is found in the specification, for example, at page 10, lines 7-14; page 17, lines 19-21; and page 30, line 28 to page 31, line 9. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 9, lines 21-23; page 12, lines 18-26; page 26, lines 6-19; and page 52, lines 18-20.

Claims 5-7 have been amended to recite "wherein said administration comprises a single or divided 0.1 - 50 mg/kg dose...." Support is found in the specification, for example, at page 59, line 18 to page 60, line 7. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 10, line 22 to page 11, line 9 and page 41, line 3-13.

Claims 1-7 and 18-19 have been further amended to recite "anti-TNFα." Support is found in the specification, for example, at page 16, lines 13-24. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 10, line 22 to page 11, line 4.

Claims 1, 2 and 3, as amended, and new Claims 26-28 recite "ATCC Accession No. PTA-7045." Support is found in the specification, as amended, for example, at page 25, lines 15-22. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Claim 15 has been amended to alter dependency since Claim 8 was canceled. Claim 15, as amended, recites "the method of Claim 1 further comprising administering to the human an effective amount of a pain control agent." Support for this amendment is found in Claim 15 as originally-filed.

New Claim 20 recites the method of Claim 5 wherein said single or divided dose is one selected from 0.5, 0.9, 1, 1.1, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 mg/kg per day on at least one of day 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or at least one of week 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16,

17, 18, 19 or 20. Support is found in the specification, for example, at page 59, line 26 to page 60, line 7. In addition, support is found in the specification of priority application US Serial No. 07/943,852, filed September 11, 1992, for example, at page 42, lines 5-18.

New Claim 21 recites "the method of Claim 1, wherein said Scatchard analysis comprises labeling the anti-TNFα antibody or antigen-binding fragment thereof and measuring direct binding of ^{125}I labeled anti-TNFα antibody or antigen-binding fragment thereof to immobilized rhTNFα, and wherein said antibodies are labelled to a specific activity of about 9.7 μCi/μg by the iodogen method." Support is found in the specification, for example, at Example X, particularly page 79, line 28 to page 80, line 11. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at Example X, particularly page 67, line 12 to page 68, line 18.

New Claim 22 is directed to the method of Claim 1, wherein the anti-TNFα antibody or antigen-binding fragment comprises a human constant region and a human variable region. Support is found in the specification, for example, at page 9, lines 8-11; page 30, line 28 to page 31, line 9. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

New Claim 23 is directed to the method of Claim 1, which comprises at least one human light chain and at least one human heavy chain. Support is found in the specification, for example, at page 19, lines 1-6; and page 30, line 28 to page 31, line 9. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25.

New Claim 24 is directed to the method of Claim 1, wherein said anti-TNFα antibody or antigen-binding fragment is administered to the human by means of parenteral administration. New Claim 25 is directed to the method of Claim 1 wherein said anti-TNFα antibody or antigen-binding fragment is administered to the human by means of intravenous administration, subcutaneous administration or intramuscular administration. Support is found in the specification, for example, at page 59, lines 5-11. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 40, lines 18-21.

New Claims 26 recites "wherein the light chain comprises all antigen-binding regions of

the light chain of A2 (ATCC Accession No. PTA-7045)." New Claim 27 recites " wherein the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045)." New Claim 28 recites "wherein the light chain comprises all antigen-binding regions of the light chain of A2 (ATCC Accession No. PTA-7045) and the heavy chain comprises all antigen-binding regions of the heavy chain of A2 (ATCC Accession No. PTA-7045)." Support is found in the specification, for example, at page 25, lines 15-22 and page 26, line 28 to page 27, line 12. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 8-25, page 19, lines 14-20; page 21, lines 11-21; and page 23, line 14 to page 24, line 2.

New Claim 29 is directed to "a composition comprising the anti-TNFα antibody or antigen-binding fragment of Claim 1, and a pharmaceutically acceptable carrier." Support is found in the specification, for example, at page 60, line 26 to page 61, line 14. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 40, line 22 to page 42, line 9.

New Claim 30 is directed to "the method of Claim 1, wherein the anti-TNFα antibody or antigen-binding fragment thereof has specificity for a neutralizing epitope of human TNFα." Support is found in the specification, for example, at page 9, lines 21-24 and page 10, lines 7-14. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 12, lines 18-25.

New Claim 31 is directed to the method of Claim 1, wherein said anti-TNFα antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:5. New Claim 32 is directed to the method of Claim 31, wherein the non-human variable region is murine. New Claim 33 is directed to the method of Claim 32, wherein the non-human variable region comprises a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4. Support is found in the specification, for example, at page 12, lines 15-18; page 25, lines 15-22; and Figures 16A-16B. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 19, lines 14-20. As discussed below, the biological deposit for the A2 antibody (designation c134A) with American Type Culture collection (ATCC) under the Budapest Treaty, was deposited on September 22,

2005. The Federal Circuit has held that reference in the specification to a deposit in a public depository, which makes its contents accessible to the public, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of section 112. *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 966 (Fed. Cir. 2002). The *Enzo* court reasoned that a person of skill in the art, reading the accession numbers in the patent specification, can obtain the claimed sequences from the ATCC depository by following the appropriate techniques to excise the nucleotide sequences from the deposited organisms containing those sequences. Thus, the court concluded that "reference in the specification to deposits of nucleotide sequences describe those sequences sufficiently to the public for purposes of meeting the written description requirement." *Id.* at 965-966.

No new matter has been added. Therefore, entry of the amendments into the application is respectfully requested.

Amendments to the Specification

The title and abstract have been amended to recite "Methods of Treating Neurodegenerative Disease with Anti-TNF Antibodies" to be more descriptive of the claims, as amended. Support is found in the specification, for example, at page 16, lines 13-24; page 56, line 28 to page 59, line 10; particularly page 57, line 25 to page 58, line 15. In addition, support is found in the specification of priority application US Serial No. 07/670,827, filed March 18, 1991, for example, at page 39, line 20 to page 40, line 9.

Applicants have amended the specification to comply with the requirement to indicate trademarks and to correct typographical errors.

Applicants have amended the specification to correct the obvious error in the spelling of "Geysen." Applicants submit evidence that the correct spelling is "Geysen" in the enclosed Abstract (Geysen, H.M. *et al.*, "A Synthetic Strategy for Epitope Mapping", *Peptides, Proceedings of the Tenth American Peptide Symposium* 519-523 (Garland R. Marshall ed., Escom, Leiden, 1988) (Exhibit A)).

Applicants have also amended the specification to recite "ATCC Accession No. PTA-7045," and to recite that c134A was deposited pursuant to the Budapest Treaty requirements with

the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on September 22, 2005. Support for these amendments is found in the specification, as amended, for example, at page 25, lines 15-22. In addition, support for reference to the cell line for the A2 antibody is found in the priority application US Serial No. 07/670,827, filed March 18, 1991, at page 19, lines 14-20.

Filed concurrently herewith is a Statement Under 37 C.F.R. §1.804, §1.806 and §1.808.

No new matter has been added. Therefore, entry of the amendments into the application is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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